

=> save all  
ENTER NAME OR (END):109987930/L  
L# LIST L1-L23 HAS BEEN SAVED AS 'L09987930/L'

=> d his

(FILE 'HOME' ENTERED AT 14:00:54 ON 17 SEP 2003)

FILE 'REGISTRY' ENTERED AT 14:01:02 ON 17 SEP 2003

FILE 'CAPLUS' ENTERED AT 14:01:09 ON 17 SEP 2003

L1 1 S WO9937305/PN  
SELECT L1 1 RN

FILE 'REGISTRY' ENTERED AT 14:01:43 ON 17 SEP 2003

L2 1 S E1  
L3 1 S E2  
L4 1 S E3  
L5 1 S E4  
L6 1 S E5  
L7 1 S E6  
L8 1 S E7  
L9 1 S E8  
L10 1 S E9  
L11 1 S E10

FILE 'CAPLUS' ENTERED AT 14:04:11 ON 17 SEP 2003

L12 2 S US6342496/PN  
SELECT L12 1 RN

FILE 'REGISTRY' ENTERED AT 14:06:33 ON 17 SEP 2003

L13 1 S E34  
L14 1 S E21  
L15 1 S E36  
L16 1 S E37  
L17 1 S E38  
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L19 1 S E51  
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L21 1 S E19  
L22 1 S E12  
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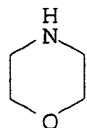
SAVE ALL L09987930/L

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E1 1 106083-71-0/BI  
E2 1 124-68-5/BI  
E3 1 15481-39-7/BI  
E4 1 192374-14-4/BI  
E5 1 192374-15-5/BI  
E6 1 233600-52-7/BI  
E7 1 233600-53-8/BI  
E8 1 233600-54-9/BI  
E9 1 34841-35-5/BI  
E10 1 34911-51-8/BI  
E11 2 109889-09-0/BI  
E12 2 112727-80-7/BI  
E13 2 34911-55-2/BI  
E14 2 364-62-5/BI  
E15 2 83863-69-8/BI  
E16 2 89565-68-4/BI  
E17 2 90182-92-6/BI  
E18 2 99614-02-5/BI  
E19 1 102141-11-7/BI

E29	1	291275-46-2/BI
E30	1	292055-71-1/BI
E31	1	292055-72-2/BI
E32	1	31677-93-7/BI
E33	1	32634-66-5/BI
E34	1	34841-35-5/BI
E35	1	34911-51-8/BI
E36	1	357399-43-0/BI
E37	1	357399-44-1/BI
E38	1	357628-59-2/BI
E39	1	357628-60-5/BI
E40	1	357628-62-7/BI
E41	1	357628-63-8/BI
E42	1	357628-64-9/BI
E43	1	357637-16-2/BI
E44	1	357637-18-4/BI
E45	1	386210-39-5/BI
E46	1	386210-40-8/BI
E47	1	386210-41-9/BI
E48	1	50-67-9/BI
E49	1	51-41-2/BI
E50	1	51-61-6/BI
E51	1	80478-42-8/BI
E52	1	80478-43-9/BI
E53	1	82801-49-8/BI
E54	1	87-69-4/BI
E55	1	92264-81-8/BI
E56	1	92264-82-9/BI
E57	1	99102-04-2/BI

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 146420-18-0 REGISTRY  
CN **Morpholinol** (9CI) (CA INDEX NAME)  
MF C4 H9 N O2  
CI IDS  
SR CA  
LC STN Files: BIOSIS, CA, CAPLUS



D1-OH

2 REFERENCES IN FILE CA (1937 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1937 TO DATE)

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=> d sel e12-

E12	2	112727-80-7/BI
E13	2	34911-55-2/BI
E14	2	364-62-5/BI
E15	2	83863-69-8/BI
E16	2	89565-68-4/BI
E17	2	90182-92-6/BI
E18	2	99614-02-5/BI
E19	1	102141-11-7/BI
E20	1	102141-12-8/BI
E21	1	106083-71-0/BI
E22	1	124-68-5/BI
E23	1	153365-82-3/BI
E24	1	18162-48-6/BI
E25	1	192374-14-4/BI
E26	1	192374-15-5/BI
E27	1	287477-53-6/BI
E28	1	291275-45-1/BI
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E52	1	80478-43-9/BI
E53	1	82801-49-8/BI
E54	1	87-69-4/BI
E55	1	92264-81-8/BI
E56	1	92264-82-9/BI
E57	1	99102-04-2/BI

=>

L16 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN

RN 357399-44-1 REGISTRY

CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with  
(2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol (1:1) (9CI) (CA  
INDEX NAME)

OTHER CA INDEX NAMES:

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)-,  
(2R,3R)-2,3-bis[(4-methylbenzoyl)oxy]butanedioate (1:1) (salt) (9CI)

FS STEREOSEARCH

MF C20 H18 O8 . C13 H18 Cl N O2

SR CA

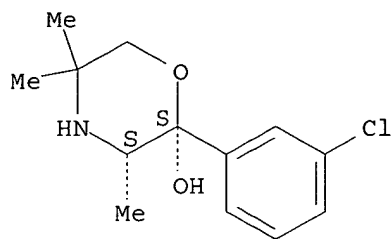
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 192374-14-4

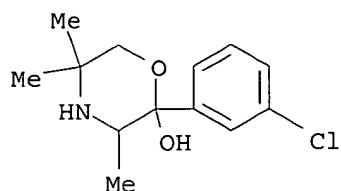
CMF C13 H18 Cl N O2

Absolute stereochemistry. Rotation (+).



CM 2

L15 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 357399-43-0 REGISTRY  
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl- (9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN 2-Hydroxy-2-(3-chlorophenyl)-3,5,5-trimethylmorpholine  
FS 3D CONCORD  
MF C13 H18 Cl N O2  
SR CA  
LC STN Files: CA, CAPLUS, CHEMCATS, USPATFULL

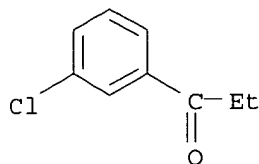


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1937 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1937 TO DATE)

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L13 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 34841-35-5 REGISTRY  
CN 1-Propanone, 1-(3-chlorophenyl)- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Propiophenone, 3'-chloro- (6CI, 7CI)  
OTHER NAMES:  
CN 1-(3-Chlorophenyl)-1-propanone  
CN 3-Chlorophenyl ethyl ketone  
CN m-Chloropropiophenone  
FS 3D CONCORD  
MF C9 H9 Cl O  
LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS,  
CHEMINFORMRX, CHEMLIST, CSCHEM, IFICDB, IFIPAT, IFIUDB, MSDS-OHS, PROMT,  
SPECINFO, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL  
(\*File contains numerically searchable property data)  
Other Sources: EINECS\*\*  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

44 REFERENCES IN FILE CA (1937 TO DATE)  
44 REFERENCES IN FILE CAPLUS (1937 TO DATE)  
9 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

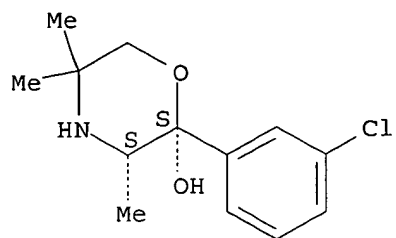
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L14 1 106083-71-0/BI

=> d

L14 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
RN 106083-71-0 REGISTRY  
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride,  
(2S,3S)- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride,  
[S-(R\*,R\*)]-  
OTHER NAMES:  
CN BW 306U  
FS STEREOSEARCH  
MF C13 H18 Cl N O2 . Cl H  
SR CA  
LC STN Files: BIOSIS, CA, CAPLUS, DDFU, DRUGU, TOXCENTER, USPAT2, USPATFULL  
CRN (192374-14-4)

Absolute stereochemistry. Rotation (+).



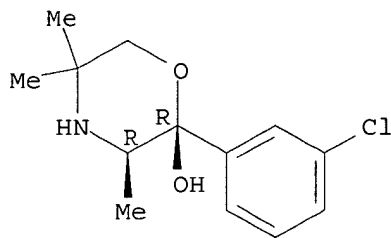
● HCl

9 REFERENCES IN FILE CA (1937 TO DATE)  
9 REFERENCES IN FILE CAPLUS (1937 TO DATE)



L23 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN  
 RN 192374-15-5 REGISTRY  
 CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA  
 INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R-cis)-  
 OTHER NAMES:  
 CN (-)-(2R,3R)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol  
 FS STEREOSEARCH  
 MF C13 H18 Cl N O2  
 CI COM  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

9 REFERENCES IN FILE CA (1937 TO DATE)  
 9 REFERENCES IN FILE CAPLUS (1937 TO DATE)

=>

L25 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN  
 AN 2003:334659 CAPLUS  
 DN 138:343887  
 TI Pharmaceutical compositions containing morpholinol deriv.  
 IN Partridge, John Joseph  
 PA USA  
 SO U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U. S. 6,391,875.  
 CODEN: USXXCO  
 DT Patent  
 LA English  
 IC ICM A61K031-535  
 NCL 514238800  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1, 4, 31

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003083330	A1	20030501	US 2002-150287	20020517
	US 6274579	B1	20010814	US 1999-233531	19990120
	US 2002019396	A1	20020214	US 2001-886391	20010622
	US 6391875	B2	20020521		
	US 2003027827	A1	20030206	US 2002-147588	20020517
PRAI	US 1999-233531	A3	19990120		
	US 2001-886391	A2	20010622		
	GB 1998-1230	A	19980121		
	US 1998-72180P	P	19980122		
AB	A compn. contains (+)-(2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol (I) and salts and solvates thereof. A method of treating depression, attention deficit hyperactivity disorder (ADHD), obesity, migraine, pain, sexual dysfunction, Parkinson's disease, Alzheimer's disease, addiction to cocaine or nicotine-contg. (esp. tobacco) products, or addiction to alc. using such a compd. is also disclosed. Results from the tetrabenazine-induced behavioral depression model showed that in vivo at 25 mg/kg (i.p.), I and the racemate, abolished the tetrabenazine-induced behavioral depression. In contrast, the (-) enantiomer of I showed only modest activity.				
ST	morpholinol pharmaceutical antidepressant alcoholism prepn; chlorophenyltrimethylmorpholinol pharmaceutical alcoholism prepn				
IT	Absolute configuration Alcoholism Antidepressants Drug delivery systems (pharmaceutical compns. contg. morpholinol deriv.)				
IT	Synopsis (synaptosome; pharmaceutical compns. contg. morpholinol deriv.)				
IT	<b>233600-52-7P</b> RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (in morpholinol deriv. prepn.; pharmaceutical compns. contg. morpholinol deriv.)				
IT	<b>192374-15-5P</b> RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (in morpholinol deriv. prepn.; pharmaceutical compns. contg. morpholinol deriv.)				
IT	124-68-5, 2-Amino-2-methyl-1-propanol 15481-39-7, Dioxane dibromide 34841-35-5 RL: RCT (Reactant); RACT (Reactant or reagent) (in morpholinol deriv. prepn.; pharmaceutical compns. contg. morpholinol deriv.)				
IT	<b>233600-54-9P</b> 517866-72-7P				

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(in morpholinol deriv. prepn.; pharmaceutical compns. contg. morpholinol deriv.)

IT 106083-71-0P 192374-14-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(pharmaceutical compns. contg. morpholinol deriv.)

IT 233600-53-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(pharmaceutical compns. contg. morpholinol deriv.)

IT 50-67-9, Serotonin, biological studies 51-41-2, Noradrenaline 51-61-6, Dopamine, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study) (uptake; pharmaceutical compns. contg. morpholinol deriv.)

IT 233600-52-7P

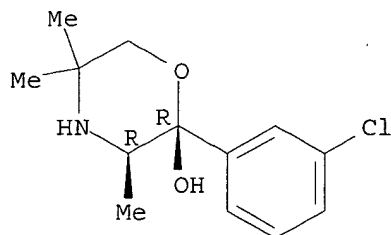
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(in morpholinol deriv. prepn.; pharmaceutical compns. contg. morpholinol deriv.)

RN 233600-52-7 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 192374-15-5P

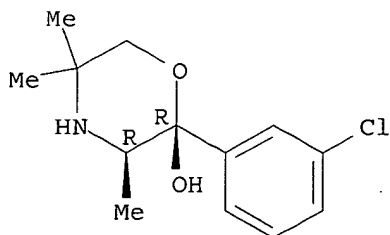
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(in morpholinol deriv. prepn.; pharmaceutical compns. contg. morpholinol deriv.)

RN 192374-15-5 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 233600-54-9P

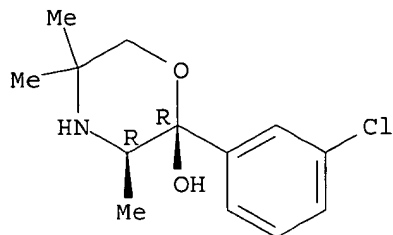
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(in morpholinol deriv. prepn.; pharmaceutical compns. contg. morpholinol deriv.)

RN 233600-54-9 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2R,3R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

IT 106083-71-0P 192374-14-4P

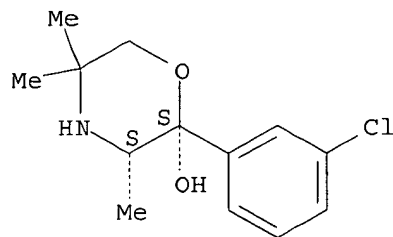
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(pharmaceutical compns. contg. morpholinol deriv.)

RN 106083-71-0 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

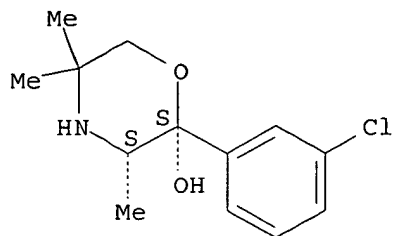


● HCl

RN 192374-14-4 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 233600-53-8P

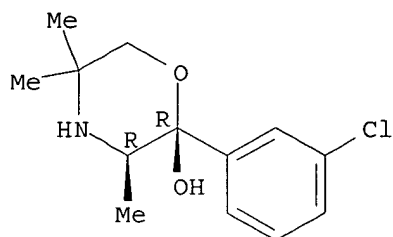
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(pharmaceutical compns. contg. morpholinol deriv.)

RN 233600-53-8 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

L25 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2003:261022 CAPLUS

DN 138:265672

TI Pharmaceutically active morpholinol, preparation, pharmaceutical compositions, and therapeutic use

IN Morgan, Phillip Frederick; Musso, David Lee; Partridge, John Joseph

PA USA

SO U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. 6,391,875.

CODEN: USXXCO

DT Patent

LA English

IC ICM A61K031-537

NCL 514238800

CC 1-11 (Pharmacology)

Section cross-reference(s): 28, 63

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003064988	A1	20030403	US 2002-150339	20020517
	US 6274579	B1	20010814	US 1999-233531	19990120
	US 2002019396	A1	20020214	US 2001-886391	20010622
	US 6391875	B2	20020521		
	US 2003027827	A1	20030206	US 2002-147588	20020517
PRAI	US 1999-233531	A3	19990120		
	US 2001-886391	A2	20010622		
	GB 1998-1230	A	19980121		
	US 1998-72180P	P	19980122		

AB The invention discloses the compd. (+)-(2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol and pharmaceutically acceptable salts and solvates thereof, pharmaceutical compns. comprising them, and processes for their prepn. and use. Also disclosed is a method of treating depression, attention deficit hyperactivity disorder (ADHD), obesity, migraine, pain, sexual dysfunction, Parkinson's disease, Alzheimer's disease, or addiction to cocaine or nicotine-contg. (esp. tobacco) products using the above compd., salts, solvates, or compns. The compd. of the invention (prepn. and resoln. described) is an enantiomer of a bupropion metabolite.

ST bupropion metabolite enantiomer morpholinol deriv prepn pharmaceutical; attention deficit hyperactivity disorder morpholinol deriv; depression obesity migraine pain morpholinol deriv; sexual dysfunction Parkinson disease morpholinol deriv; Alzheimer disease cocaine addiction morpholinol deriv; tobacco nicotine product addiction morpholinol deriv

IT Mental disorder  
(bipolar disorder; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Analgesics  
Antidepressants  
Antimigraine agents  
Antiparkinsonian agents  
Pain  
Parkinson's disease  
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Resolution (separation)  
(chromatog.; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Mental disorder  
(depression; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Sexual behavior  
(disorder; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Toxicity  
(drug; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Behavior  
(locomotor, disorder; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Mental disorder  
(major depression; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Headache  
(migraine; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Behavior  
(motor, disorder; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Nerve, disease  
(neuropathy, neuropathic pain; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Drug dependence  
(nicotine-contg. product; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT Biological transport  
(uptake, sexual dysfunction as selective serotonin reuptake inhibitor-class antidepressant side effect; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT **233600-52-7P**  
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT 192374-15-5P  
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT 192374-14-4P  
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT 31677-93-7, Wellbutrin 34911-55-2, Bupropion  
 RL: PAC (Pharmacological activity); BIOL (Biological study)  
 (bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT 106083-71-0P  
 RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT 233600-54-9P  
 RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)  
 (bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT 124-68-5, 2-Amino-2-methyl-1-propanol 15481-39-7, Dioxane dibromide 34841-35-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT 34911-51-8P, 2-Bromo-3'-chloropropiophenone 233600-53-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

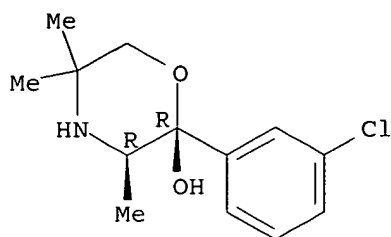
IT 54-11-5, Nicotine  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
 (nicotine-contg. product addiction; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT 50-67-9, Serotonin, biological studies 51-41-2, Noradrenaline 51-61-6, Dopamine, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (uptake; bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

IT 233600-52-7P  
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
 (bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

RN 233600-52-7 CAPLUS  
 CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)-rel- (9CI)  
 (CA INDEX NAME)

Relative stereochemistry.



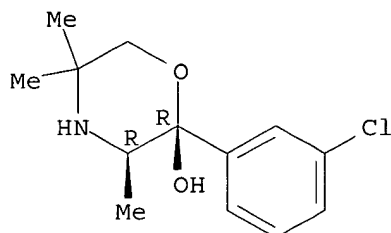
IT 192374-15-5P

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

RN 192374-15-5 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



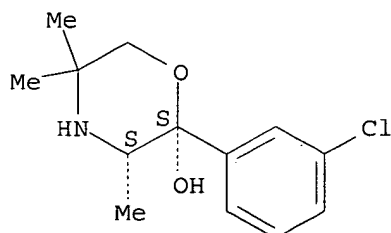
IT 192374-14-4P

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

RN 192374-14-4 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



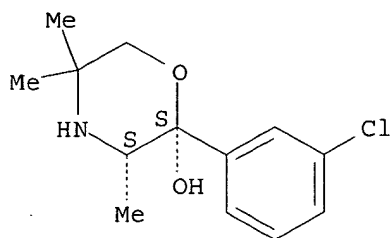
IT 106083-71-0P

RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)



RN 106083-71-0 CAPLUS  
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride,  
(2S,3S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

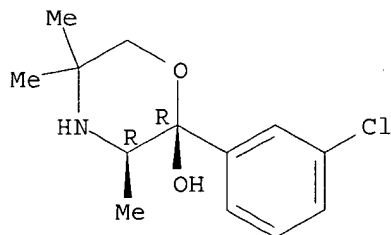


● HCl

IT 233600-54-9P  
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)  
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

RN 233600-54-9 CAPLUS  
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride,  
(2R,3R) - (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

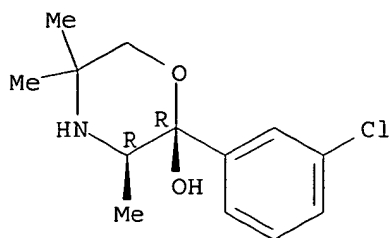


● HCl

IT 233600-53-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(bupropion metabolite enantiomer morpholinol deriv. prepn. and therapeutic use)

RN 233600-53-8 CAPLUS  
CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride,  
(2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

L25 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN  
 AN 2003:173828 CAPLUS  
 DN 138:218798  
 TI Polymorphisms in genes associated with norepinephrine function and their use in the design and selection of therapies  
 IN Dow, David J.; Duncan, Ben; Hughes, Arlene R.; Manasco, Penelope; Pillai, Sreekumar G.; Spaulding, Theodore C.; Spraggs, Colin F.; Stubbins, Michael; Xu, Chun-Fang  
 PA Smithkline Beecham Corporation, USA  
 SO PCT Int. Appl., 205 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C12Q001-68  
 ICS C07H021-04  
 CC 13-6 (Mammalian Biochemistry)  
 Section cross-reference(s): 1, 3  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003018843	A1	20030306	WO 2002-US25060	20020807
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003100479	A1	20030529	US 2002-213948	20020807
PRAI	US 2001-313918P	P	20010821		
	US 2001-337819P	P	20011108		
AB	Correlations between the appearance of polymorphisms in various genes and a subject's phenotypic response to treatment with a norepinephrine reuptake inhibitor are described. Methods of screening subjects to aid in the medical treatment of obesity are presented. Polymorphisms are described in genes for monoamine oxidase B, the NET1 norepinephrine transporter, the DAT1 dopamine transporter, the D2 dopamine receptor, the serotonin transporter and the NR1 NMDA receptor. Clin. studies between the effectiveness of the antiobesity agents GW320659 and GW353162 and genotypes at these loci are presented.				
ST	obesity norepinephrine reuptake polymorphism obesity treatment				
IT	Dopamine receptors				
	RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				

(D2, polymorphisms in gene for; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Gene, animal  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (G155A, polymorphisms in; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Gene, animal  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (G6435A, polymorphisms in; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Gene, animal  
 Gene, animal  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (NET1, polymorphisms in; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Glutamate receptors  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (NMDA-binding, NMDAR-1, polymorphisms in gene for; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Gene, animal  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (NR1, polymorphisms in; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Gene, animal  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (T342C, polymorphisms in; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Repetitive DNA  
 RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (VNTR (variable-no. tandem-repeat), polymorphism in, as indicator of effectiveness of antiobesity agents; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Transport proteins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (dopamine-transporting, DAT1, polymorphisms in gene for; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Obesity  
 (genotyping in selection of treatment for; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Antiobesity agents  
 (genotyping in selection of; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Monoamines  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibitors of reuptake of, polymorphisms and therapeutic effectiveness of; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Body weight  
(loss, therapeutic induction of in treatment of obesity; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Transport proteins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(norepinephrine transporter, NET1, polymorphisms in gene for; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Heart rate  
(polymorphisms affecting response to antiobesity drugs of; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Alleles  
Genetic polymorphism  
Genotyping (method)  
Human  
(polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Transport proteins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(serotonin transporter, polymorphisms in gene for; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT Genetic polymorphism  
(single nucleotide; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT 9001-66-5  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(B, polymorphisms in gene for; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT 50-67-9, Serotonin, biological studies 51-41-2, Norepinephrine  
51-61-6, Dopamine, biological studies  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(inhibitors of reuptake of, polymorphisms and therapeutic effectiveness of; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT 135306-42-2 **192374-14-4**  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polymorphisms and therapeutic effectiveness of; polymorphisms in genes assocd. with norepinephrine function and their use in design and selection of therapies)

IT 152316-08-0, GenBank Z29071 154899-20-4, GenBank X76753 165758-41-8, GenBank Z32772 165758-43-0, GenBank Z32774 391536-08-6, GenBank M95167 391548-92-8, GenBank X76758 391548-96-2, GenBank X76762 391772-54-6, GenBank X91127 391854-90-3, GenBank U79746 392067-92-4, GenBank AF050737 398113-85-4, GenBank X91119 398113-92-3, GenBank X91126  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(polymorphisms in genes assocd. with norepinephrine function and their use in the design and selection of therapie)

IT 500753-96-8, 1: PN: WO03018843 SEQID: 1 unclaimed DNA 500753-97-9, 2: PN: WO03018843 SEQID: 2 unclaimed DNA 500753-98-0, 3: PN: WO03018843 SEQID: 3 unclaimed DNA 500753-99-1, 4: PN: WO03018843 SEQID: 4 unclaimed DNA 500754-00-7, 5: PN: WO03018843 SEQID: 5 unclaimed DNA 500754-01-8,

6: PN: WO03018843 SEQID: 6 unclaimed DNA 500754-02-9, 7: PN: WO03018843  
 SEQID: 7 unclaimed DNA 500754-03-0, 8: PN: WO03018843 SEQID: 8 unclaimed  
 DNA 500754-04-1, 9: PN: WO03018843 SEQID: 9 unclaimed DNA 500754-05-2  
 500754-06-3 500754-07-4 500754-08-5 500754-09-6 500754-10-9  
 500754-11-0 500754-12-1 500754-13-2 500754-14-3 500754-15-4  
 500754-16-5 500754-17-6 500754-18-7 500754-19-8 500754-20-1  
 500754-21-2 500754-22-3 500754-23-4 500754-24-5 500754-25-6  
 500754-26-7 500754-27-8 500754-28-9 500754-29-0 500754-30-3  
 500754-31-4 500754-32-5 500754-33-6 500754-34-7

RL: PRP (Properties)

(unclaimed nucleotide sequence; polymorphisms in genes assocd. with  
 norepinephrine function and their use in the design and selection of  
 therapies)

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Bertrand; J AM ACAD CHILD ADOLESC PSYCHIATRY 1999, V38(12), P1474
- (2) Eriksson; Alcohol 2001, V24(1), P15 CAPLUS
- (3) Ho; Annals of Neurology 1995, V37(3), P403 CAPLUS
- (4) Mundo; American Journal of Medical Genetics (Neuropsychiatric Genetics)  
 2000, V96, P379 MEDLINE
- (5) Okabe; The Journal of Neuroscience 1999, V19(18), P7781 CAPLUS
- (6) Rosmond; Journal of Human Hypertension 2001, V15, P553 CAPLUS
- (7) Serritti; Psychiatry Research 2001, V104, P195
- (8) Stober; American Journal of Medical Genetics (Neuropsychiatric Genetics)  
 1996, V67, P523 MEDLINE

IT 192374-14-4

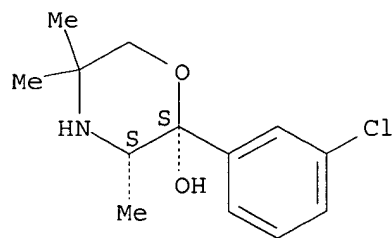
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(polymorphisms and therapeutic effectiveness of; polymorphisms in genes  
 assocd. with norepinephrine function and their use in design and  
 selection of therapies)

RN 192374-14-4 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry. Rotation (+).



L25 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2003:118594 CAPLUS

DN 138:147756

TI Pharmaceutically active morpholinol

IN Ascher, John A.; Johnston, Joseph Andrew; Learned-Coughlin, Susan Marie;  
 Bye, Alan

PA USA

SO U.S. Pat. Appl. Publ., 10 pp., Cont.-in-part of U.S. Ser. No. 886,391.  
 CODEN: USXXCO

DT Patent

LA English

IC ICM A61K031-537

NCL 514238500

CC 1-11 (Pharmacology)

Section cross-reference(s): 28

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003032643	A1	20030213	US 2002-150341	20020517
	US 6274579	B1	20010814	US 1999-233531	19990120
	US 2002019396	A1	20020214	US 2001-886391	20010622
	US 6391875	B2	20020521		
	US 2003027827	A1	20030206	US 2002-147588	20020517
PRAI	US 1999-233531	A3	19990120		
	US 2001-886391	A2	20010622		
	GB 1998-1230	A	19980121		
	US 1998-72180P	P	19980122		
AB	Disclosed is the compd. (+)-(2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol and pharmaceutically acceptable salts and solvates thereof, pharmaceutical compns. comprising them, and processes for their prepn.; also disclosed is a method of treating depression, attention deficit hyperactivity disorder (ADHD), obesity, migraine, pain, sexual dysfunction, Parkinson's disease, Alzheimer's disease, addiction to cocaine or tobacco products, seasonal affective disorder, chronic fatigue, narcolepsy or cognitive impairment using such compd., salts, solvates or compns.				
ST	morpholinol deriv prepn antidepressant chronic fatigue treatment; seasonal affective disorder treatment morpholinol deriv				
IT	Mental disorder (affective, seasonal; prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)				
IT	Resolution (separation) (chromatog.; prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)				
IT	Fatigue, biological (chronic fatigue syndrome; prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)				
IT	Mental disorder (cognitive; prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)				
IT	Mental disorder (depression; prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)				
IT	Cognition (disorder; prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)				
IT	Sleep (narcolepsy; prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)				
IT	Absolute configuration Antidepressants Brain Cognition enhancers (prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)				
IT	192374-14-4P RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)				

(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT 106083-71-0P

RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT 192374-15-5P, (-)-(2R,3R)-2-(3-Chlorophenyl)-3,5,5-trimethyl-2-morpholinol 233600-52-7P 233600-53-8P 233600-54-9P

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT 50-67-9, Serotonin, biological studies 51-41-2, Noradrenaline 51-61-6, Dopamine, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT 124-68-5, 2-Amino-2-methyl-1-propanol 34841-35-5

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT 34911-51-8P, 2-Bromo-3'-chloropropiophenone

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

IT 192374-14-4P

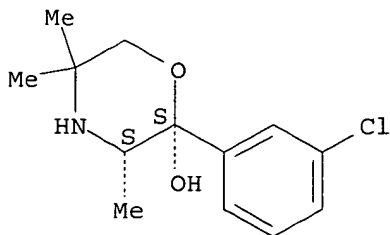
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

RN 192374-14-4 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 106083-71-0P

RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of

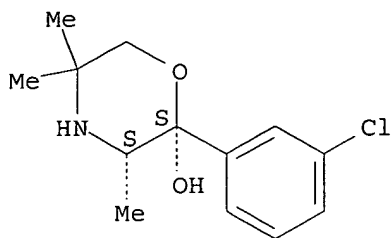
action); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

RN 106083-71-0 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HCl

IT 192374-15-5P, (-)-(2R,3R)-2-(3-Chlorophenyl)-3,5,5-trimethyl-2-morpholinol 233600-52-7P 233600-53-8P

233600-54-9P

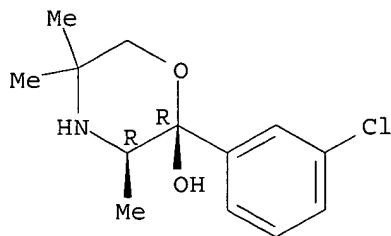
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of pharmaceutically active morpholinol to treat mental disorders such as seasonal affective disorder in relation to effect on monamine uptake in brain and toxicity)

RN 192374-15-5 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

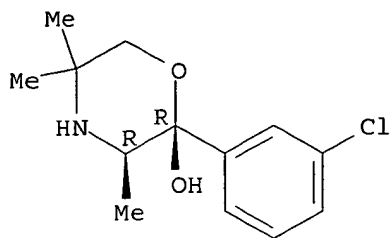


RN 233600-52-7 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

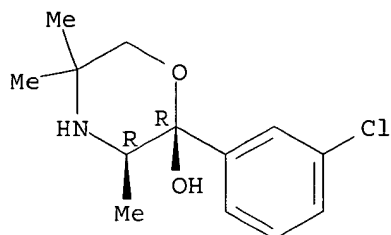




RN 233600-53-8 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride,  
(2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

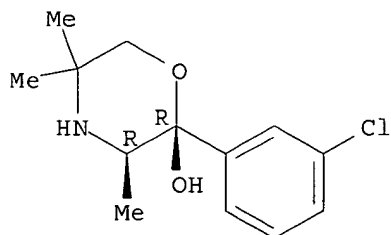


● HCl

RN 233600-54-9 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride,  
(2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

L25 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2002:23847 CAPLUS

DN 136:79797

TI Bupropion metabolites, and preparation thereof, for treatment of sexual dysfunction

IN Fang, Qun Kevin; Senanayake, Chrisantha Hugh; Grover, Paul

PA Sepracor, Inc., USA

SO U.S., 26 pp., Cont.-in-part of U.S. 510,241.

CODEN: USXXAM

DT Patent

LA English  
 IC ICM A61K031-535  
 ICS A61K031-135  
 NCL 514231200  
 CC 1-12 (Pharmacology)  
 Section cross-reference(s): 25, 63  
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6337328	B1	20020108	US 2000-640725	20000818
	US 6342496	B1	20020129	US 2000-510241	20000222
	WO 2001062257	A2	20010830	WO 2000-US23080	20000823
	WO 2001062257	A3	20020704		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	EP 1259243	A2	20021127	EP 2000-957684	20000823
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
	US 2002052340	A1	20020502	US 2001-987930	20011116
	US 2002052341	A1	20020502	US 2001-987931	20011116
PRAI	US 1999-122277P	P	19990301		
	US 1999-148324P	P	19990811		
	US 2000-510241	A2	20000222		
	US 2000-640725	A	20000818		
	WO 2000-US23080	W	20000823		
AB	Methods are disclosed which use metabolites of bupropion (prepn. described) for treating sexual dysfunction. Tablet formulations are included.				
ST	bupropion metabolite prepn sexual dysfunction treatment; tablet pharmaceutical bupropion metabolite sexual dysfunction				
IT	5-HT antagonists (5-HT3; bupropion metabolite prepn. for treatment of sexual dysfunction)				
IT	Antiemetics Resolution (separation) (bupropion metabolite prepn. for treatment of sexual dysfunction)				
IT	Sexual behavior (disorder; bupropion metabolite prepn. for treatment of sexual dysfunction)				
IT	Sexual behavior (impotence; bupropion metabolite prepn. for treatment of sexual dysfunction)				
IT	Drug delivery systems (mucosal; bupropion metabolite prepn. for treatment of sexual dysfunction)				
IT	Drug delivery systems (oral; bupropion metabolite prepn. for treatment of sexual dysfunction)				
IT	Sexual behavior (premature ejaculation; bupropion metabolite prepn. for treatment of sexual dysfunction)				
IT	Drug delivery systems (tablets; bupropion metabolite prepn. for treatment of sexual dysfunction)				
IT	Drug delivery systems (transdermal; bupropion metabolite prepn. for treatment of sexual dysfunction)				
IT	Vagina				

(vaginal dryness and vaginismus; bupropion metabolite prepn. for treatment of sexual dysfunction)

IT 50-67-9, Serotonin, biological studies 51-41-2, Norepinephrine 51-61-6, Dopamine, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (bupropion metabolite prepn. for treatment of sexual dysfunction)

IT 102141-11-7P 102141-12-8P 153365-82-3P 292055-72-2P  
**357399-43-0P**  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (bupropion metabolite prepn. for treatment of sexual dysfunction)

IT **192374-14-4P 192374-15-5P**  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (bupropion metabolite prepn. for treatment of sexual dysfunction)

IT 364-62-5, Metoclopramide 364-62-5D, Metoclopramide, stereoisomers and metabolites 34911-55-2D, Bupropion, metabolites 82801-49-8 83863-69-8, Norcisapride 83863-69-8D, Norcisapride, stereoisomers and metabolites 89565-68-4, Tropisetron 89565-68-4D, Tropisetron, stereoisomers and metabolites 90182-92-6, Zacopride 90182-92-6D, Zacopride, stereoisomers and metabolites 92264-81-8 99614-02-5, Ondansetron 99614-02-5D, Ondansetron, stereoisomers and metabolites 109889-09-0, Granisetron 109889-09-0D, Granisetron, stereoisomers and metabolites 112727-80-7, Renzapride 112727-80-7D, Renzapride, stereoisomers and metabolites 357628-59-2 357628-60-5 386210-40-8 386210-41-9  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (bupropion metabolite prepn. for treatment of sexual dysfunction)

IT 80478-42-8P 80478-43-9P **106083-71-0P** 292055-71-1P 357628-62-7P 357637-16-2P 357637-18-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation) (bupropion metabolite prepn. for treatment of sexual dysfunction)

IT 34911-51-8P 92264-82-9P 99102-04-2P 291275-45-1P 291275-46-2P **357399-44-1P** 357628-63-8P 357628-64-9P 386210-39-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. and reaction; bupropion metabolite prepn. for treatment of sexual dysfunction)

IT 87-69-4, L-Tartaric acid, reactions 124-68-5, 2-Amino-2-methyl-1-propanol 18162-48-6 31677-93-7, Bupropion hydrochloride 32634-66-5, Di-p-toluoyl-L-tartaric acid 34841-35-5 34911-55-2, Bupropion 287477-53-6  
 RL: RCT (Reactant); RACT (Reactant or reagent) (reaction; bupropion metabolite prepn. for treatment of sexual dysfunction)

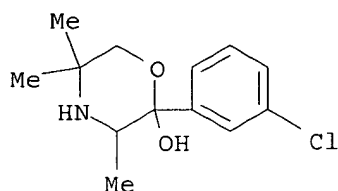
RE.CNT 143 THERE ARE 143 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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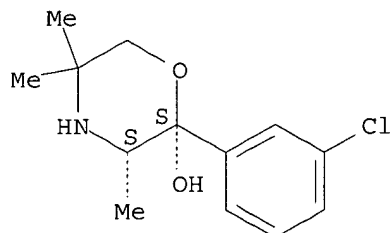
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 IT 357399-43-0P  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (bupropion metabolite prepn. for treatment of sexual dysfunction)  
 RN 357399-43-0 CAPLUS  
 CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl- (9CI) (CA INDEX NAME)



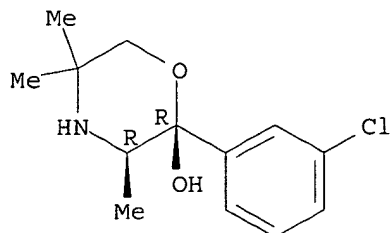
IT 192374-14-4P 192374-15-5P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (bupropion metabolite prepn. for treatment of sexual dysfunction)  
 RN 192374-14-4 CAPLUS  
 CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 192374-15-5 CAPLUS  
 CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



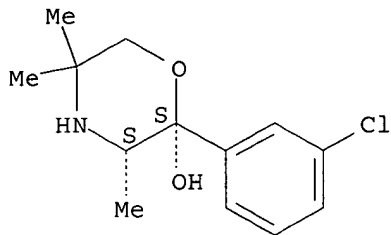
IT 106083-71-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(bupropion metabolite prepn. for treatment of sexual dysfunction)

RN 106083-71-0 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride,  
(2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HCl

IT 357399-44-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(prepn. and reaction; bupropion metabolite prepn. for treatment of  
sexual dysfunction)

RN 357399-44-1 CAPLUS

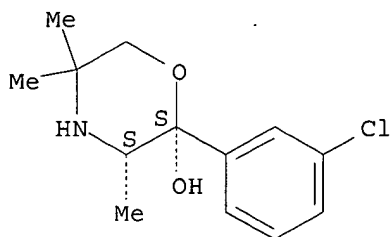
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with  
(2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol (1:1) (9CI) (CA  
INDEX NAME)

CM 1

CRN 192374-14-4

CMF C13 H18 Cl N O2

Absolute stereochemistry. Rotation (+).

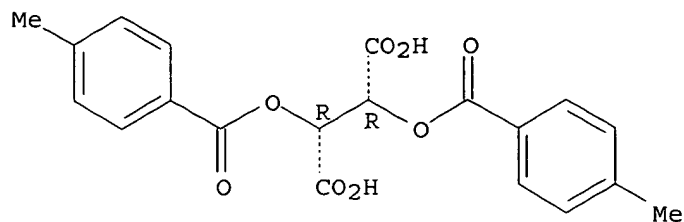


CM 2

CRN 32634-66-5

CMF C20 H18 O8

Absolute stereochemistry.



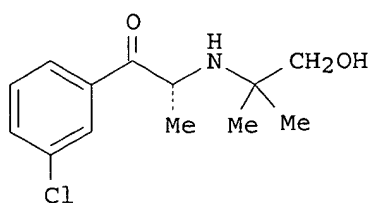
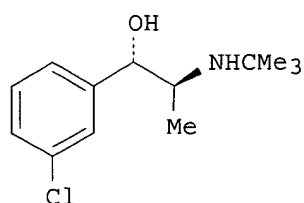
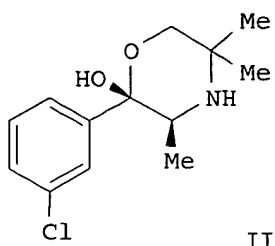
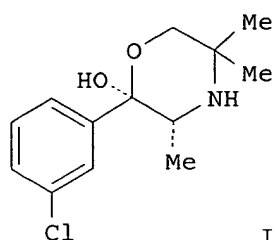
L25 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN  
 AN 2001:635898 CAPLUS  
 DN 135:211043  
 TI Synthesis of bupropion metabolites and their use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake  
 IN Fang, Qun K.; Senanayake, Chrisantha H.; Grover, Paul  
 PA Sepracor Inc., USA  
 SO PCT Int. Appl., 69 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-5375  
 ICS A61K031-137; A61P025-24; A61P025-34; A61P025-20  
 CC 28-13 (Heterocyclic Compounds (More Than One Hetero Atom))  
 Section cross-reference(s): 1, 63

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001062257	A2	20010830	WO 2000-US23080	20000823
	WO 2001062257	A3	20020704		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	US 6342496	B1	20020129	US 2000-510241	20000222
	US 6337328	B1	20020108	US 2000-640725	20000818
	EP 1259243	A2	20021127	EP 2000-957684	20000823
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
PRAI	US 2000-510241	A	20000222		
	US 2000-640725	A	20000818		
	US 1999-122277P	P	19990301		
	US 1999-148324P	P	19990811		
	WO 2000-US23080	W	20000823		

GI





- AB Methods and compns. are disclosed which utilize metabolites of bupropion, including optically pure metabolites, e.g. I, II, III and IV, for treating disorders ameliorated by inhibition of neuronal monoamine reuptake, such as, sexual dysfunction, affective disorders, cerebral function disorders, cigarette smoking, and urinary incontinence. Thus, III was prepd. from racemic bupropion hydrochloride via borane redn.; resoln. of the racemic threo deriv. with L-tartaric acid to isolate the (R,R)-stereoisomer as the L-tartrate salt; treatment of supernatant with D-tartaric acid to give the (S,S)-stereoisomer as the D-tartrate salt; and hydrolysis of the latter to give III. III was tested for inhibition of inhibition of 5-HT reuptake [insignificant results, IC<sub>50</sub> = 229 nM (nH = 0.8)].
- ST bupropion metabolite prepn neuronal monoamine reuptake inhibitor; sexual dysfunction treatment bupropion metabolite; cerebral function disorder treatment bupropion metabolite; cigarette smoking disorder treatment bupropion metabolite; incontinence treatment bupropion metabolite
- IT 5-HT antagonists  
(5-HT<sub>3</sub>, adjunct medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)
- IT Muscarinic receptors  
Nicotinic receptors  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(antagonists, adjunct medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)
- IT Brain  
(cerebral dysfunction, medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)
- IT Tobacco products  
(cigarettes, nicotine addiction, medicaments; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)
- IT Mental disorder  
(depression, medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)
- IT Sexual behavior  
(disorder, medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

reuptake)

IT Sexual behavior  
(impotence, medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT Bladder  
(incontinence, medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT Alzheimer's disease  
Epilepsy  
Parkinson's disease  
(medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT Sleep  
(narcolepsy, medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT Monoamines  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(neuronal, reuptake inhibitor; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT 5-HT antagonists  
(serotonin reuptake inhibitor adjunct medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT Analgesics  
Anti-inflammatory agents  
Anticonvulsants  
Antidepressants  
Drug delivery systems  
(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT 54-11-5, Nicotine  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(adjunct medicament; synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT 357399-44-1P 357628-61-6P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT 80478-42-8P 80478-43-9P 92264-82-9P 99102-04-2P 102141-11-7P  
102141-12-8P 153365-82-3P 192374-14-4P 292055-72-2P  
357628-62-7P 357628-64-9P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT 31677-93-7 34911-55-2, (.+-.)-Bupropion  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT 34911-55-2DP, Bupropion, metabolites and derivs. **106083-71-0P**  
**192374-15-5P 233600-54-9P** 292055-71-1P 357399-46-3P  
 357399-47-4P 357628-59-2P 357628-60-5P 357628-63-8P 357637-16-2P  
 357637-18-4P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT 75-64-9, tert-Butylamine, reactions 87-69-4, L-Tartaric acid, reactions 124-68-5, 2-Amino-2-methyl-1-propanol 147-71-7, D-Tartaric acid 32634-66-5 32634-68-7 34841-35-5, 1-(3-Chlorophenyl)-1-propanone 287477-53-6  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT 34911-51-8P, 2-Bromo-3'-chloropropiophenone 291275-45-1P 291275-46-2P **357399-43-0P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

IT **357399-44-1P**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

RN 357399-44-1 CAPLUS

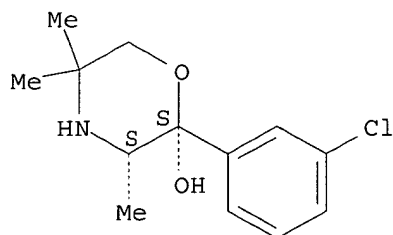
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with (2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 192374-14-4

CMF C13 H18 Cl N O2

Absolute stereochemistry. Rotation (+).

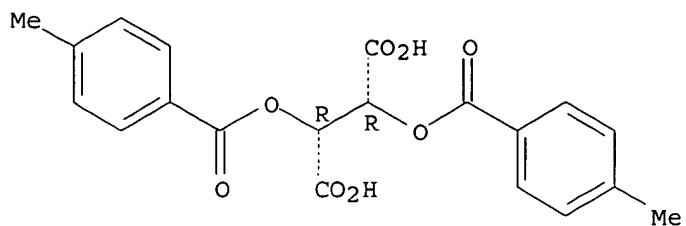


CM 2

CRN 32634-66-5

CMF C20 H18 O8

Absolute stereochemistry.



IT 192374-14-4P

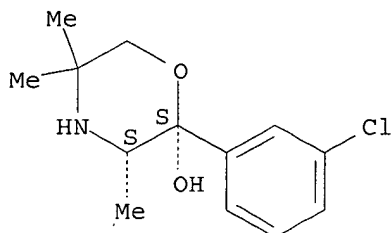
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

RN 192374-14-4 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 106083-71-0P 192374-15-5P 233600-54-9P

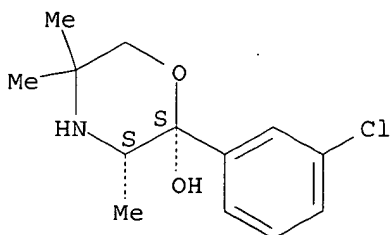
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of bupropion metabolites and use for treating disorders ameliorated by inhibition of neuronal monoamine reuptake)

RN 106083-71-0 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

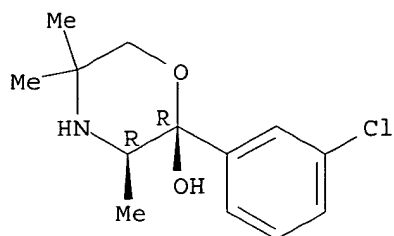


● HCl

RN 192374-15-5 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

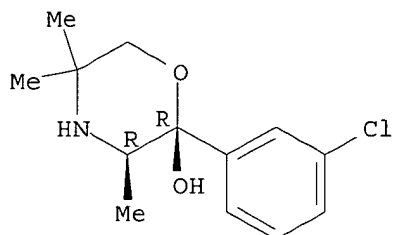
Absolute stereochemistry. Rotation (-).



RN 233600-54-9 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride,  
(2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

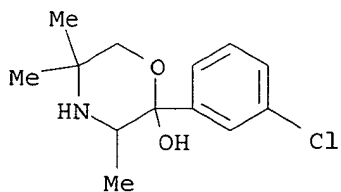
IT 357399-43-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

(synthesis of bupropion metabolites and use for treating disorders  
ameliorated by inhibition of neuronal monoamine reuptake)

RN 357399-43-0 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl- (9CI) (CA INDEX NAME)



L25 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN

AN 2000:836391 CAPLUS

DN 134:147365

TI Rapid access to enantiopure bupropion and its major metabolite by  
stereospecific nucleophilic substitution on an .alpha.-keto triflate

AU Fang, Q. K.; Han, Z.; Grover, P.; Kessler, D.; Senanayake, C. H.; Wald, S.  
A.

CS Chemical Process Research and Development, Sepracor Inc., Marlborough, MA,  
01752, USA

SO Tetrahedron: Asymmetry (2000), 11(18), 3659-3663

CODEN: TASYE3; ISSN: 0957-4166

PB Elsevier Science Ltd.

DT Journal

LA English

CC 25-16 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

Section cross-reference(s): 63

OS CASREACT 134:147365

AB A stereospecific method for the synthesis of enantiopure .alpha.-amino ketone from its corresponding .alpha.-hydroxy ketone via a triflate intermediate is discussed. This strategy provides a rapid and efficient route for the prepn. of either enantiomer of bupropion and its biol. active hydroxylated metabolite. To a soln. of (2R)-1-(3-chlorophenyl)-2-hydroxy-1-propanone (0.30 g) in dichloromethane (6 mL) was added trifluoromethanesulfonic acid anhydride (0.50 g) at -78.degree.; then, lutidine (0.26 g) was added. The intermediate trifluoromethanesulfonic acid (1R)-2-(3-chlorophenyl)-1-methyl-2-oxoethyl ester (.alpha.-keto triflate) was not isolated. The reaction mixt. was allowed to warm to -40.degree. and stirred at that temp. for 40 min before 2-amino-2-methyl-1-propanol (0.40 g) was added. This mixt. was stirred at -40.degree. for 2 h, warmed to 0.degree. and stirred overnight. After work-up, the product, (+)-(2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol, was obtained in 65% yield and 98% enantiomeric excess.

ST stereoselective nucleophilic substitution keto triflate; trifluoromethanesulfonate chlorophenyloxoethyl prepn nucleophilic substitution; propanone trifluoromethylsulfonyloxy stereochem nucleophilic substitution aminopropanol; chlorophenyl morpholinol bupropion metabolite prepn; bupropion Wellbutrin prepn

IT Stereochemistry

(prepn. of bupropion and its metabolite by stereoselective nucleophilic substitution of trifluoromethanesulfonic acid (chlorophenyl)methyl(oxo)ethyl ester)

IT Substitution reaction, nucleophilic

(stereoselective; prepn. of bupropion and its metabolite by stereoselective nucleophilic substitution of trifluoromethanesulfonic acid (chlorophenyl)methyl(oxo)ethyl ester)

IT 75-64-9, tert-Butylamine, reactions 124-68-5, 2-Amino-2-methyl-1-propanol 358-23-6, Trifluoromethanesulfonic acid anhydride 287477-53-6 291275-46-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of bupropion and its metabolite by stereoselective nucleophilic substitution of trifluoromethanesulfonic acid (chlorophenyl)methyl(oxo)ethyl ester)

IT 192374-14-4P, (+)-(2S,3S)-2-(3-Chlorophenyl)-3,5,5-trimethyl-2-morpholinol 192374-15-5P, (-)-(2R,3R)-2-(3-Chlorophenyl)-3,5,5-trimethyl-2-morpholinol 324548-43-8P, (S)-Bupropion 324548-45-0P, (S)-Bupropion hydrochloride

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of bupropion and its metabolite by stereoselective nucleophilic substitution of trifluoromethanesulfonic acid (chlorophenyl)methyl(oxo)ethyl ester)

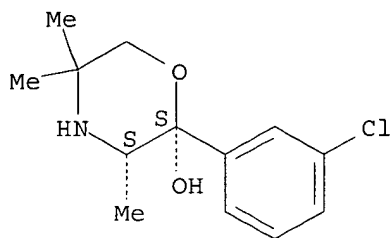
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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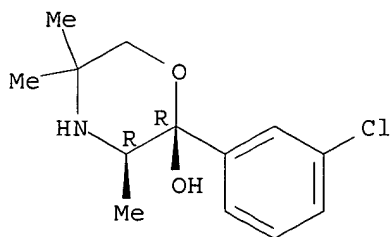
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 (22) Zhu, Y; Tetrahedron Lett 1998, V39, P7819 CAPLUS  
 IT 192374-14-4P, (+)-(2S,3S)-2-(3-Chlorophenyl)-3,5,5-trimethyl-2-morpholinol 192374-15-5P, (-)-(2R,3R)-2-(3-Chlorophenyl)-3,5,5-trimethyl-2-morpholinol  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of bupropion and its metabolite by stereoselective nucleophilic substitution of trifluoromethanesulfonic acid  
 (chlorophenyl)methyl(oxo)ethyl ester)  
 RN 192374-14-4 CAPLUS  
 CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 192374-15-5 CAPLUS  
 CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L25 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN  
 AN 2000:627938 CAPLUS  
 DN 133:227784  
 TI Bupropion metabolites and methods of their synthesis and therapeutic uses and compositions  
 IN Jerussi, Thomas P.; McCullough, John R.; Senanayake, Chrisantha H.; Fang, Qun K.  
 PA Sepracor Inc., USA  
 SO PCT Int. Appl., 41 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English

ICI A61  
CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 1, 25  
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000051546	A2	20000908	WO 2000-US5109	20000229
	WO 2000051546	A3	20010111		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 2000035055	A5	20000921	AU 2000-35055	20000229
PRAI	US 1999-122277P	P	19990301		
	US 1999-148324P	P	19990811		
	WO 2000-US5109	W	20000229		
OS	MARPAT 133:227784				
AB	Methods and compns. are disclosed which utilize metabolites of bupropion for treating disorders ameliorated by inhibition of neuronal monoamine reuptake. Such disorders include, but are not limited to, erectile dysfunction, affective disorders, cerebral function disorders, cigarette smoking, and incontinence. The invention further discloses methods of making optically pure bupropion metabolites.				
ST	bupropion metabolite synthesis treatment monoamine reuptake disorder; erectile dysfunction treatment bupropion metabolite; affective disorder treatment bupropion metabolite; cigarette smoking treatment bupropion metabolite; incontinence treatment bupropion metabolite; optically pure bupropion metabolite				
IT	5-HT antagonists (5-HT3, adjunctive administration with; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)				
IT	Antiemetics (adjunctive administration with; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)				
IT	Mental disorder (affective, treatment of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)				
IT	Anticonvulsants Antidepressants Antiparkinsonian agents (bupropion metabolites and methods of synthesis and therapeutic uses and compns.)				
IT	Drug delivery systems (capsules; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)				
IT	Brain, disease (cerebrum, treatment of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)				
IT	Mental disorder (depression, treatment of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)				
IT	Sexual behavior (impotence, treatment of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)				
IT	Bladder (incontinence, treatment of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)				
IT	Drug delivery systems (mucosal; bupropion metabolites and methods of synthesis and				



therapeutic uses and compns.)

IT Sleep  
(narcolepsy, treatment of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Drug delivery systems  
(oral; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Behavior  
(smoking, cessation of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Drug delivery systems  
(solids; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Drug delivery systems  
(solns.; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Drug delivery systems  
(tablets; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Drug delivery systems  
(transdermal patches; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Drug delivery systems  
(transdermal; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Nerve  
(treating disorder ameliorated by inhibition of monoamine reuptake in; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Monoamines  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(treating disorder ameliorated by inhibition of neuronal reuptake of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Epilepsy  
Parkinson's disease  
(treatment of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT Biological transport  
(uptake, treating disorder ameliorated by inhibition of neuronal monoamine reuptake; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 364-62-5, Metoclopramide 89565-68-4, Tropisetron 90182-92-6, Zacopride 99614-02-5, Ondansetron 109889-09-0, Granisetron 112727-80-7, Renzapride  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(adjunctive administration with; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 34911-55-2, Bupropion 119802-68-5 292055-72-2  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 153365-82-3P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 102141-12-8P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 358-23-6, Trifluoromethane sulfonic anhydride  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 124-68-5, 2-Amino-2-methyl-1-propanol 34841-35-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 291275-45-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 287477-53-6P 291275-46-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 192374-15-5P 292055-71-1P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 34911-55-2DP, Bupropion, metabolites  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 291275-47-3 291275-48-4 291275-49-5 291275-50-8 291275-51-9 291275-52-0  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 51-41-2, Norepinephrine  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (inhibition of reuptake of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 50-67-9, Serotonin, biological studies  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (second pharmacol. active compds. of inhibitors of reuptake of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 51-61-6, Dopamine, biological studies  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (treating disorder ameliorated by inhibition of neuronal reuptake of; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

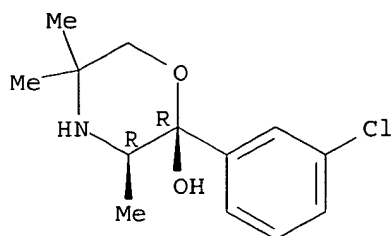
IT 54-11-5, Nicotine  
 RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (treatment of addiction to; bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

IT 192374-15-5P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (bupropion metabolites and methods of synthesis and therapeutic uses and compns.)

RN 192374-15-5 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L25 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN  
AN 1999:487216 CAPLUS  
DN 131:111445  
TI Pharmaceutically active morpholinol  
IN Morgan, Phillip Frederick; Musso, David Lee; Partridge, John Joseph  
PA Glaxo Group Limited, UK  
SO PCT Int. Appl., 23 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
IC ICM A61K031-535  
CC 1-11 (Pharmacology)  
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9937305	A1	19990729	WO 1999-US1134	19990120
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2318268	AA	19990729	CA 1999-2318268	19990120
	AU 9923280	A1	19990809	AU 1999-23280	19990120
	AU 755536	B2	20021212		
	BR 9907203	A	20001017	BR 1999-7203	19990120
	EP 1047428	A1	20001102	EP 1999-903200	19990120
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
	EE 200000438	A	20011217	EE 2000-438	19990120
	JP 2002501025	T2	20020115	JP 2000-528287	19990120
	NZ 505809	A	20020927	NZ 1999-505809	19990120
	NO 2000003721	A	20000919	NO 2000-3721	20000720
	HR 2000000494	A1	20001231	HR 2000-494	20000721
PRAI	GB 1998-1230	A	19980121		
	US 1998-72180P	P	19980122		
	WO 1999-US1134	W	19990120		
AB	Disclosed are the compd. (+)-(2S,3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol and pharmaceutically acceptable salts and solvates thereof, pharmaceutical compns. comprising them, and a method of treating depression, attention deficit hyperactivity disorder (ADHD), obesity, migraine, pain, sexual dysfunction, Parkinson's disease, Alzheimer's disease, or addiction to cocaine or nicotine-contg. (esp. tobacco) products using such compd., salts, solvates or compns.				
ST	bupropion metabolite morpholinol dextro enantiomer antidepressant				
IT	Mental disorder				

(attention deficit hyperactivity disorder; pharmaceutically active morpholinol compd.)

IT Sexual behavior  
(disorder; pharmaceutically active morpholinol compd.)

IT Analgesics  
Anti-Alzheimer's agents  
Antidepressants  
Antimigraine agents  
Antiobesity agents  
Antiparkinsonian agents  
Drug dependence  
(pharmaceutically active morpholinol compd.)

IT 106083-71-0P 192374-14-4P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(pharmaceutically active morpholinol compd.)

IT 124-68-5, 2-Amino-2-methyl-1-propanol 15481-39-7, Dioxane dibromide 34841-35-5  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of pharmaceutically active morpholinol compd.)

IT 34911-51-8P, 2-Bromo-3'-chloropropiophenone 233600-52-7P 233600-53-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of pharmaceutically active morpholinol compd.)

IT 192374-15-5P 233600-54-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of pharmaceutically active morpholinol compd.)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

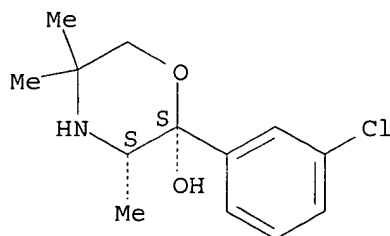
RE  
(1) Kelley; J Med Chem 1996, V39(2), P347 CAPLUS  
(2) Martin, P; Pharmacopsychiatry 1990, V23(4), P187 MEDLINE

IT 106083-71-0P 192374-14-4P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(pharmaceutically active morpholinol compd.)

RN 106083-71-0 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

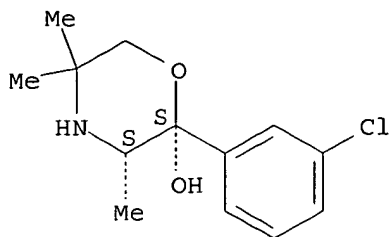


● HCl

RN 192374-14-4 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 233600-52-7P 233600-53-8P

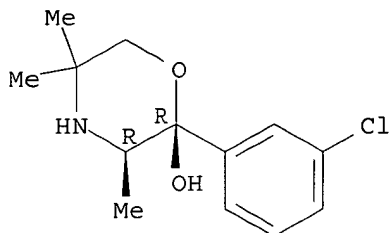
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of pharmaceutically active morpholinol compd.)

RN 233600-52-7 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)-rel- (9CI)  
(CA INDEX NAME)

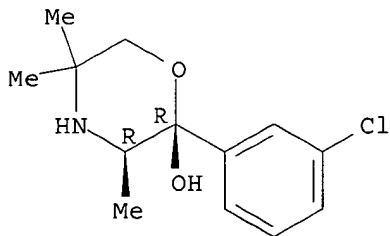
Relative stereochemistry.



RN 233600-53-8 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride,  
(2R,3R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

IT 192374-15-5P 233600-54-9P

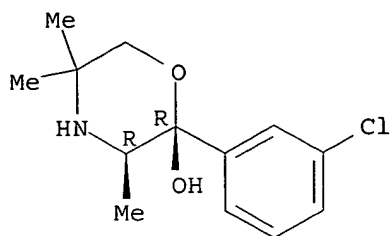
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of pharmaceutically active morpholinol compd.)

RN 192374-15-5 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

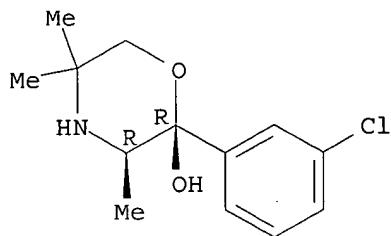
Absolute stereochemistry. Rotation (-).



RN 233600-54-9 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride,  
(2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

L25 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1997:375543 CAPLUS

DN 127:103838

TI Enantiomeric determination of the phenylmorpholinol metabolite of  
bupropion in human plasma using coupled achiral-chiral liquid  
chromatography

AU Suckow, Raymond F.; Zhang, Ming F.; Cooper, Thomas B.

CS Analytical Psychopharmacology Division, New York State Psychiatric  
Institute, New York, NY, 10032, USA

SO Biomedical Chromatography (1997), 11(3), 174-179

CODEN: BICHE2; ISSN: 0269-3879

PB Wiley

DT Journal

LA English

CC 1-1 (Pharmacology)

AB A coupled achiral-chiral stationary phase liq. chromatog. technique was  
developed to sep. and quantitate the enantiomers of the phenylmorpholinol  
metabolite (2) of the antidepressant bupropion (1) in human plasma. At  
the retention time of 2, a switching valve loaded a portion of the eluting  
compd. onto a protein-bonded chiral stationary phase which resolved 2 into  
the (+) (-) stereoisomers using an aq. mobile phase of potassium phosphate  
(pH=6.25) and 5% 2-propanol. All eluting compds. were monitored using UV  
detection at 214 nm, and no plasma endogenous material or other commonly  
used psychotropic drugs were found to interfere. Within-day and  
between-day variations were less than 6% over the expected concn. range,  
and a limit of quantitation of about 125 ng/mL of 2 was obsd.

Steady-state plasma samples from 17 patients receiving 1 were found to  
contain the (-) enantiomer to the extent of about 96% of total 2. The  
potential clin. implications of these results are not known since all  
previous pharmacol. studies were carried out with the racemic 2.

ST bupropion phenylmorpholinol metabolite enantiomer detn plasma; liq

chromatog bupropion metabolite enantiomer detn

IT Blood analysis  
Resolution (separation)  
(bupropion phenylmorpholinol metabolite enantiomeric detn. in human plasma by coupled achiral-chiral liq. chromatog.)

IT 192374-14-4 192374-15-5  
RL: ANT (Analyte); BSU (Biological study, unclassified); MFM (Metabolic formation); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative)  
(bupropion phenylmorpholinol metabolite enantiomeric detn. in human plasma by coupled achiral-chiral liq. chromatog.)

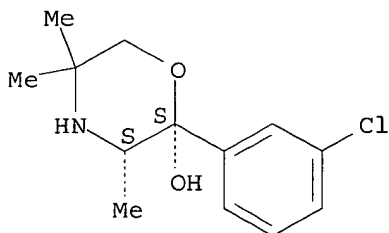
IT 31677-93-7, Bupropion hydrochloride  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(bupropion phenylmorpholinol metabolite enantiomeric detn. in human plasma by coupled achiral-chiral liq. chromatog.)

IT 192374-14-4 192374-15-5  
RL: ANT (Analyte); BSU (Biological study, unclassified); MFM (Metabolic formation); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative)  
(bupropion phenylmorpholinol metabolite enantiomeric detn. in human plasma by coupled achiral-chiral liq. chromatog.)

RN 192374-14-4 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2S,3S)- (9CI) (CA INDEX NAME)

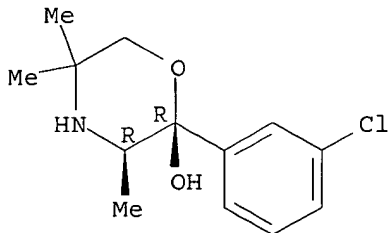
Absolute stereochemistry. Rotation (+).



RN 192374-15-5 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L25 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1996:6865 CAPLUS

DN 124:146028

TI (2S,3S,5R)-2-(3,5-Difluorophenyl)-3,5-dimethyl-2-morpholinol: A Novel Antidepressant Agent and Selective Inhibitor of Norepinephrine Uptake

AU Kelley, James L.; Musso, David L.; Boswell, G. Evan; Soroko, Francis E.; Cooper, Barrett R.

CS Division of Organic Chemistry, Burroughs Wellcome Co., Research Triangle Park, NC, 27709, USA

SO Journal of Medicinal Chemistry (1996), 39(2), 347-9  
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

CC 28-13 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1

AB The title compd. was prepd. in four steps from 3,5-difluorobenzonitrile. The pharmacol. profile of (2S,3S,5R)-2-(3,5-difluorophenyl)-3,5-dimethyl-2-morpholinol suggests that it will display antidepressant activity which involves inhibition of the norepinephrine uptake mechanism without the cholinergic or cardiac depression effects assocd. with tricyclic antidepressants.

ST norepinephrine difluorophenyl dimethyl morpholinol prepn; antidepressant difluorophenyl dimethyl morpholinol prepn

IT Antidepressants  
(prepn. of (difluorophenyl)dimethylmorpholinol as antidepressant and selective inhibitor of norepinephrine uptake)

IT 106083-71-0, BW 306U  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(prepn. of)

IT 135306-39-7P 135306-42-2P, BW 1555U88 135306-47-7P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. of (difluorophenyl)dimethylmorpholinol as antidepressant and selective inhibitor of norepinephrine uptake)

IT 64248-63-1, 3,5-Difluorobenzonitrile  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of (difluorophenyl)dimethylmorpholinol as antidepressant and selective inhibitor of norepinephrine uptake)

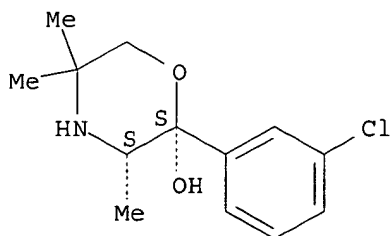
IT 135306-45-5P, 1-(3,5-Difluorophenyl)-1-propanone 135306-46-6P, 2-Bromo-1-(3,5-difluorophenyl)-1-propanone 173069-02-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of (difluorophenyl)dimethylmorpholinol as antidepressant and selective inhibitor of norepinephrine uptake)

IT 106083-71-0, BW 306U  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(prepn. of)

RN 106083-71-0 CAPLUS

CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

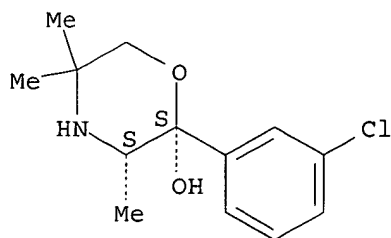


● HCl



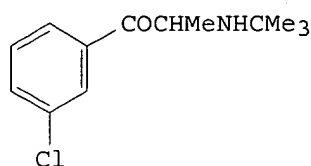
L25 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1987:400205 CAPLUS  
 DN 107:205  
 TI Pharmacological significance of the species differences in bupropion metabolism  
 AU Welch, Richard M.; Lai, Allen A.; Schroeder, David H.  
 CS Wellcome Res. Lab., Research Triangle Park, NC, 27560, USA  
 SO Xenobiotica (1987), 17(3), 287-98  
 CODEN: XENOBH; ISSN: 0049-8254  
 DT Journal  
 LA English  
 CC 1-2 (Pharmacology)  
 AB Bupropion was previously shown to provide a dose-dependent prevention of tetrabenazine-induced sedation in mice but not rats. Bupropion was extensively metabolized in mice, rats, dogs and man. About 85% of the dose was excreted in the urine of rats and man. The predominant metabolites in rat urine were side chain cleavage products of bupropion [m-chlorobenzoic acid] with a minor fraction consisting of basic side chain hydroxylated metabolites. Mice, dogs and man form a major side chain hydroxylated product BW 306U which appeared in higher concns. than bupropion in plasma of these species but not rats. The relatively high plasma levels of BW 306U in mice but not rats may account for the species difference in pharmacol. response obsd. with bupropion.  
 ST bupropion metab species; antidepressant action bupropion species  
 IT Mental disorder  
 (depression, inhibition of, species difference in bupropion metab. in humans and lab. animals in relation to)  
 IT 535-80-8, m-Chlorobenzoic acid 34911-55-2D, Bupropion, glucuronide conjugates 57728-59-3 80478-42-8 80478-43-9 **106083-71-0**, B.W. 306U  
 RL: FORM (Formation, nonpreparative)  
 (formation of, as bupropion metabolite, in humans and lab. animals, species differences in)  
 IT 34911-55-2, Bupropion  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (metab. of, in humans and lab. animals, species differences in, pharmacol. significance of)  
 IT **106083-71-0**, B.W. 306U  
 RL: FORM (Formation, nonpreparative)  
 (formation of, as bupropion metabolite, in humans and lab. animals, species differences in)  
 RN 106083-71-0 CAPLUS  
 CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● HCl

L25 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1987:43388 CAPLUS  
 DN 106:43388  
 TI Pharmacokinetics of bupropion and metabolites in plasma and brain of rats, mice, and guinea pigs  
 AU Suckow, Raymond F.; Smith, Thomas M.; Perumal, Arthur S.; Cooper, Thomas B.  
 CS Dep. Anal. Psychopharmacol., New York State Psychiatr. Inst., Orangeburg, NY, 10962, USA  
 SO Drug Metabolism and Disposition (1986), 14(6), 692-7  
 CODEN: DMDSAI; ISSN: 0090-9556  
 DT Journal  
 LA English  
 CC 1-2 (Pharmacology)  
 GI



AB Rats, mice, and guinea pigs were used as animal models to evaluate bupropion (I) metab. The pharmacokinetics of bupropion and its major basic metabolites, BW 306U and BW A494U, were detd. by liq chromatog. following i.p. administration of 40 mg/kg bupropion. Further investigation of the reduced bupropion metabolite BW A494U was carried out by the i.p. administration of this metabolite to these animals and assaying the plasma and brain samples 90 min after dosing. Anal. of the pharmacokinetic data revealed that the rat quickly metabolized bupropion, but no basic metabolites accumulated. The mouse metabolized bupropion predominantly to BW 306U, whereas the guinea pig converted bupropion to reduced bupropion (BW A494U) as well as BW 306U. Brain to plasma ratios of bupropion among these animals did not vary significantly. However, both metabolites showed dramatic differences in their brain to plasma ratios among these species. When BW A494U was injected, almost 3% of the plasma concn. of BW A494U was detd. to be bupropion in the rat. Lesser amts. were converted in the mouse and guinea pig than in the rat. Therefore, distinct differences exist in the metab. of bupropion in various species of animals. The guinea pig, when compared to the rat or mouse, appears to constitute a model that most closely resembles that of human bupropion metab.  
 ST bupropion metabolite pharmacokinetics plasma brain  
 IT Blood plasma  
 Brain, metabolism  
 (bupropion pharmacokinetics in)  
 IT 80478-42-8 106083-71-0  
 RL: PROC (Process)  
 (as bupropion metabolite, pharmacokinetics of)  
 IT 34911-55-2, Bupropion  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (pharmacokinetics of)  
 IT 106083-71-0  
 RL: PROC (Process)  
 (as bupropion metabolite, pharmacokinetics of)  
 RN 106083-71-0 CAPLUS  
 CN 2-Morpholinol, 2-(3-chlorophenyl)-3,5,5-trimethyl-, hydrochloride, (2S,3S)- (9CI) (CA INDEX NAME)